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INFLUENCE OF AMBIENT TEMPERATURE ON THE PRODUCTION OF RESTRAINT ULCERS IN THE RAT

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16. Abstract The article describes a study of the influence of ambient temperature on the production of restraint ulcers in the rat. It concludes the production of restraint ulcers, is favored by the reduction of the environmental temperature, whether the rat had been subjected to a fast or not.			
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INFLUENCE OF AMBIENT TEMPERATURE ON THE PRODUCTION OF  
RESTRAINT ULCERS IN THE RAT\*

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See In a previous work [1] we fixed the experimental conditions in which it is possible, by using the immobilizing procedure recommended by Rossi, Bonfils et al [2], to obtain in the white rat, previously subjected to a 24 hour fast, a high percentage of experimental ulcers with a short period of restraint not surpassing two and a half hours. During these experiments, which regularly produce 82 to 85% ulcerous lesions among the animals, the rats are maintained at an ambient temperature of  $22 \pm 1^{\circ}\text{C}$ . However, in summer, during periods of high heat, without climatization, when the environmental temperature exceeds  $22^{\circ}$ , some apparently aberrant series include only a very low frequency of ulcers. These observations have justified, during the study of protective substances [3,4], the use of experimental control animals the same day. They have also led us to examine, in a systematic manner, the influence of ambient temperature on the production of restraint ulcers in the rat.

We subjected the rats to restraints of two and a half hours at different ambient temperatures ranging between  $32$  and  $14^{\circ}\text{C}$ . /1818 but constant during the duration of each experiment. We established the favorable action of cold on the frequency of the ulcers. Besides, Brodie and Valitski [5], who place the animals in an enclosure maintained in  $5-6^{\circ}\text{C}$  have already pointed out the favorable action of cold associated with a one hour restraint on the appearance of gastric hemorrhages in the rat.

It seemed of interest to us to seek to reduce the duration of the restraint to one hour and a half in the different conditions of exterior temperature and to omit the fast, whatever the duration of the restraint might be.

\* A part of these results was the object of a communication to the 85th Congress of the French Association for the Advancement of Sciences, Rouen, July 8-13, 1966. (\*) See title page

\*\* With the technical collaboration of J. Absil. (\*\*) See title page

\*\*\*Numbers in margins indicate foreign pagination.

We experiment on female rats of the Wistar breed, about six weeks old, of 110 to 120 gm in weight. The control animals and those subjected to the restraint are placed for the duration of this in an enclosure maintained at a constant temperature, fixed respectively at 32, 28, 24, 22, 19 and 14°C. In each experiment are noted: the rectal temperature of the animals at the beginning and at the end of the restraint, and the percentage of animals developing ulcers as well as the average index allowing measurement of the severity of the ulcerous damage [1].

1. PRODUCTION OF ULCERS AS A FUNCTION OF THE AMBIENT TEMPERATURE - Rats subjected to restraint after a fast of 24 hours (table 1, 1st part). - Two and a half hour restraint. - At ambient temperatures of 32, 28 and 24°, the percentage of animals developing ulcers is low, not exceeding 35%. As soon as the temperature falls below 24°, the frequency of ulcers rises regularly to reach 95% at 14°; the severity of the ulcers (average index) rises in a parallel manner. The control animals, placed in the same temperature conditions, but not subjected to restraint do not develop ulcers.

Restraint of one and a half hours. - The results are superimposable on those obtained in the animals subjected to a two and a half hour restraint. The percentage of animals bearing ulcers rises in proportion to the fall in ambient temperature: it goes from 15 to 75% while the temperature varies from 32 to 14°.

Rats subjected to restraint without prior fasting. (table 1, 2nd part). - Rats not having been subjected to a prior fast are less sensitive to the ulcerogenic action of restraint, whatever the ambient temperature might be. However, at 14° the ulcer frequency is still great: 45% after a one and a half hour restraint and 62% after a two and a half hour restraint.

One might wonder if the adjunction of the cold to the restraint, which potentiates the frequency of ulcers, leads to gastric lesions which are different or of the same nature as those obtained when the animals are maintained at the temperature at which they were raised. In order to bring some light upon this subject, we intend to examine the effects of several protective substances while the animals are maintained at variable temperatures.

II: PRODUCTION OF ULCERS AS A FUNCTION OF THE THERMAL 1819 EQUILIBRIUM (table I). - We observed running parallel to the elevation in frequency of the ulcers, especially at ambient temperatures of 19 and 14°, a significant lowering of the rectal temperature at the end of the restraint, whatever the duration might be, one and a half or two and a half hours, whether or not the animals were subjected to a prior fast. This hypothermia, whose central origin was demonstrated by Bartlett et al [6], is one of the consequences of the restraint, since the control rats who were free in the same ambient temperatures show a lesser fall in their rectal temperature.

Even though there is suppression of the hypothermia in rats placed in warmer enclosures, 32 to 28°, it does not completely prevent ulcer production (table I), and it does not 1820 seem to be the sole factor for the potentiation observed. The following experiments also work against the hypothesis of a primordial role of the hypothermia; phenobarbital (in a non-hypnotic dose) and chloral hydrate (in a hypnotic dose) which exaggerate the hypothermia due to the association of cold and restraint, clearly decreases both the frequency and the severity of ulcers.

Number of rats	Ambient temperature degrees C.	Duration of the restraint hours	% of rats presenting with ulcers	Average index $\pm$ SD:	Change in rectal temperature during the restraint degrees C.
1st part - Rats subjected to restraint after a 24 hour fast					
20	32	0	0	—	+ 1.5
70	32	2 1/2	27	0.6 $\pm$ 0.43	+ 1.7
19	28	0	0	—	0
19	28	2 1/2	21	0.32 $\pm$ 0.17	+ 0.2
18	24	0	0	—	- 0.1
20	24	2 1/2	35	0.85 $\pm$ 0.31	- 1.8
20	22	0	0	—	0
20	22	2 1/2	70	2.1 $\pm$ 0.38	- 1.6
19	19	0	0	—	- 1.2
56	19	2 1/2	86	2.89 $\pm$ 0.19	- 3.7
30	14	0	0	—	- 1
40	14	2 1/2	95	3.21 $\pm$ 0.16	- 3.5
39	32	1 1/2	15	0.23 $\pm$ 0.12	+ 2.1
40	28	1 1/2	22	0.42 $\pm$ 0.17	+ 0.4
41	19	1 1/2	66	1.78 $\pm$ 0.25	- 3.5
10	14	0	0	—	- 1.5
40	14	1 1/2	75	2.05 $\pm$ 0.50	- 2.7
2nd part - Rats subjected to restraint without a prior fast.					
20	22	2 1/2	30	0.55 $\pm$ 0.2	- 0.4
10	14	0	0	—	- 0.5
40	14	2 1/2	62.5	1.80 $\pm$ 0.4	- 3.6
20	14	1 1/2	45	0.90 $\pm$ 0.3	- 3.5

Table I.

Substances administered (dose)	% Animals bearing ulcers	Average index	Change in rectal temperature during the restraint degrees C.
Controls			
Phenobarbital (100 mg/kg)	60	1.65 $\pm$ 0.3	- 3.2
Chloral hydrate (300 mg/kg)	15	0.25 $\pm$ 0.1	- 5.5
	30	0.55 $\pm$ 0.2	- 9.3

Groups of 20 female rats, having fasted 24 hours, subjected to a one and a half hour restraint, at an ambient temperature of  $14 \pm 1^{\circ}\text{C}$ . The substances are administered by the intra-peritoneal route at the beginning of the restraint.

Table II.

### Conclusions

1. The production of restraint ulcers, whether the rat was previously subjected to a 24 hour fast or not, is favored by the lowering of the environmental temperature, notably when it is lowered from 24° to 14°C.
2. The adjunction of cold to the restraint and to the prior fast allow the duration of the restraint to be reduced from two and a half hours at 22°C. to one and a half hours at 14° to obtain ulcers with the same frequency (about 70%) and of the same severity.
3. Study of substances exercising upon the restraint ulcer either an aggravating action or a protective action of short duration, will be performed at variable ambient temperatures which delimit, as a function of the duration of the restraint more or less great frequencies of ulcers.

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